AMERICAN ACADEMY OF OPHTHALMOLOGY®

Longitudinal Visual Field and Quality-of-Life Change in the Treatment for Advanced Glaucoma Study

Giovanni Montesano, MD, PhD,[1,2] *Giovanni Ometto, PhD,*[1,2] *Riccardo Cheloni, PhD,*[1,2,3] *David F. Garway-Heath, MD,*[1] *Bethany E. Higgins, PhD,*[2] *David P. Crabb, PhD,*[2] *Anthony J. King, MD,*[4] *for the Treatment of Advanced Glaucoma Study (TAGS) Group*

Purpose: Progressive visual field (VF) loss resulting from glaucoma affects quality of life (QoL). Although treatments aim to preserve vision, the extent to which slowing VF loss translates into QoL changes in advanced disease is not understood fully. We compare the 5-year rate of VF and QoL change and examined their correlation in the Treatment for Advanced Glaucoma Study.

Design: Multicenter randomized clinical trial (27 secondary care glaucoma departments in the UK).

Participants: Adults (n = 453) with newly diagnosed advanced open-angle glaucoma in at least 1 eye were randomized to trabeculectomy (n = 227) or medical management (n = 226) as initial treatment. One eligible index eye was identified per participant.

Main Outcome Measures: Mean difference in rate of change in monocular index eye VF (24-2 SITA Standard), binocular integrated (BI) VF, and the 25-item Visual Function Questionnaire (VFQ-25) composite score over 5 years (intention to treat) using a Bayesian longitudinal hierarchical model.

Results: Data from 442 patients with reliable VF (false-positive rate ≤15%) or VFQ-25 data from >2 time points were included (221 patients in the trabeculectomy-first arm). Baseline characteristics were similar between arms. The rate of index eye VF loss was faster in the medications-first arm (−0.75 [95% credible interval (CrI), −0.90 to −0.59] dB/year) compared with the trabeculectomy-first arm (−0.37 [95% CrI, −0.53 to −0.22] dB/year; P = 0.002). Differences between groups were not statistically significant for BI VF decline (P = 0.062) or VFQ-25 change (P = 0.392). Correlations between VF and QoL were stronger for BI VF for baseline (0.41 [95% CrI, 0.32–0.49]; P < 0.001) and rate of change (0.56 [95% CrI, 0.41–0.70]; P < 0.001) than for index eye VF (0.22 [95% CrI, 0.12–0.32]; P < 0.001 and 0.43 [95% CrI, 0.26–0.58]; P < 0.001, respectively).

Conclusions: Trabeculectomy more effectively reduced the rate of VF loss compared with medical treatment in advanced glaucoma. Despite a moderately strong correlation with the BI VF, no difference was found in the measured QoL, suggesting that the VFQ-25 might not be reactive or sensitive enough to monocular glaucoma interventions.

Financial Disclosure(s): Proprietary or commercial disclosure may be found in the Footnotes and Disclosures at the end of this article. *Ophthalmology 2026;133:996-1005*

Supplemental material available at www.aaojournal.org.

Glaucoma is a pressure-related disease of the optic nerve causing progressive loss of visual field (VF) and potentially blindness. At present, intraocular pressure lowering, by means of medical treatment, laser therapy, or surgery, is the only recognized treatment to prevent further VF deterioration. Patients with advanced glaucoma have a higher risk of progressing quickly to blindness or severe visual impairment.[1–6] Maintaining quality of life (QoL) is the most important treatment outcome for glaucoma patients,[7] who are less concerned about the treatment required than they are in achieving this.[7,8]

Loss of VF has been correlated with decreased QoL in patients with glaucoma,[9–15] validating VF metrics as meaningful for patients. In recent years, researchers have attempted to measure the effect of glaucoma treatments on QoL directly. However, standardized QoL instruments have repeatedly failed to show a significant difference between treatment alternatives in randomized clinical trials, even when one treatment was clearly superior in preserving vision.[16–19]

The Treatment of Advanced Glaucoma Study (TAGS) compared medical and surgical treatment in patients with advanced glaucoma and, unlike many previous studies, was powered specifically to detect a QoL change between arms with QoL as the primary outcome.[17,18] The TAGS used the 25-item Visual Function Questionnaire (VFQ-25),[20] a validated questionnaire that has been used widely to evaluate visual outcomes in glaucoma.[19,21–23] The

http://doi.org/10.1016/j.ophtha.2026.04.020
ISSN 0161-6420/26

TAGS,[18] analyzing the average of global VF scores (mean deviation [MD]) and composite VFQ-25 QoL scores, found a clear difference in VF outcomes between the study arms, but not in QoL measurements, at 5 years.

In this analysis, we instead evaluated the differences in the rate of VF and QoL change between the 2 arms of the TAGS. Importantly, we expanded the methodology to analyze the binocular integrated (BI) VF and to quantify the correlation between VF loss and QoL. Because of the perimetric floor, MD can distort the estimates of rates of progression in advanced glaucoma.[24,25] Differently from previous analyses,[18] we use an improved methodology to account for the floor effect[25] and to provide more accurate estimates of VF rates of progression.

Methods

Patient Cohort

Details of the TAGS have been reported extensively.[26] The study was approved by the East Midlands Derby Research Ethics Committee (identifier, 13/EM/0395; registration no., ISRCTN56878850) and adhered to the tenets of the Declaration of Helsinki. All patients provided written informed consent. Briefly, the trial recruited 453 patients with newly diagnosed advanced glaucoma in at least 1 eye and randomized them to trabeculectomy or medications as the first treatment. Medical treatment was escalated according to the National Institute for Health and Care Excellence guidelines. Intraocular pressure targets were set following the Canadian Perspectives in Glaucoma Management: Setting Target Intra-Ocular Pressure Range consensus statement.[27] For all our analyses, we considered the treatment to which the patients were originally assigned (intention-to-treat analysis), although 26 participants (12%) in the trabeculectomy arm did not receive trabeculectomy in the index eye. A supplementary per-protocol analysis is reported in the Appendix (available at www.aaojournal.org).

The primary outcome of the trial was vision-related QoL measured with the VFQ-25. The VFQ-25 was administered at baseline (before randomization) and then at 4, 12, 24, 36, 48, and 60 months. Clinical effectiveness outcomes were evaluated at baseline and then at 4, 12, 24, and 60 months and included intraocular pressure, visual acuity, and VF testing (24-2 Swedish Interactive Thresholding Algorithm [SITA]-Standard; Humphrey Field Analyzer). The VF tests were performed twice at each visit.

An index eye was defined for each patient. This was the eligible eye if only 1 eye had advanced disease, or if both eyes were eligible, the eye with less severe disease according to the baseline MD value of the VF was the index eye. Both eyes received the same allocated treatment if eligible.

Data Analysis

Visual Field Data. We selected visits for which at least 1 reliable test (false-positive rate [FPR], $\leq$ 15%)[28] was available for the index eye and retained data from patients with valid data for at least 2 time points (n = 436 patients). Pointwise sensitivity values were extracted for each test and were analyzed (see below). The average of the 2 test repeats was taken at each visit, if both were reliable. The 2 blind-spot locations were excluded for the index eye analysis.

The VF data from the fellow eye of the same patients were used to calculate the BI VF. The BI VF was calculated using pointwise sensitivity values following an established methodology for binocular summation,[29] calculated as:

$$\text{Sensitivty}_{\text{binocular}} = 10 \times \log_{10}\left(\sqrt{10^{2\times(\text{Sensitivty}_{\text{right}}\,/\,10)} + 10^{2\times(\text{Sensitivty}_{\text{left}}\,/\,10)}}\right)$$

This integration rule was shown to be very similar (marginally better) compared with the best location in predicting binocular sensitivity.[29] A different set of criteria was applied to select fellow eye tests. Reliable fellow eye VFs were preferred and selected when available. Otherwise, the threshold for inclusion was raised to an FPR of $\leq$ 25% to maximize the chances that a BI VF could be calculated for all visits for which a reliable index eye VF test was available. Despite being more than the conventional 15% threshold, these test results were considered to be the best available estimate for the fellow-eye VF because of the relatively small, estimated effect of 10% increase in FPR on sensitivity.[30] However, only 7 visits in 7 patients included tests with an FPR of $>$ 15% for the fellow eye.

Only 4 visits from the fellow eye of 2 patients had no test results at less than the 25% FPR threshold. These were imputed with the best estimate from the available VF tests for the same eye (pointwise linear regression over time). This same imputation procedure was applied to visits for which no fellow eye test was available (14 visits, 10 patients). For 1 patient, no data were available for the fellow eye, which was blind, and the BI VF calculation relied on the index eye only. For the calculation of the BI VF, we included all 54 locations from the 24-2 pattern, including the blind-spot locations. The 2 temporal VF locations not tested by the 24-2 pattern were inferred from the 2 adjacent locations and were used to calculate the binocular summation.

Quality-of-Life Data. Data from patients with at least 2 VFQ-25 questionnaire results were included in the analysis (n = 439 patients). The main analysis was conducted using the composite score (range, 0–100), the main outcome measure of the trial. A secondary analysis of the individual subscales also was undertaken. All analyses were repeated using calibrated logit scores derived from the individual responses through a Rasch model. These are explained in detail and reported in the Appendix.

Longitudinal Change Analysis. A Bayesian hierarchical model was used to model the rate of the index eye VF, BI VF, and VFQ-25 scores jointly. All models were fitted using Just Another Gibbs Sampler via R software (R Foundation for Statistical Computing). Details are provided in the Appendix. For the index eye VF, the model replicated the analysis performed for the 2-year data.[25] Briefly, the hierarchical model used pointwise data to estimate the average rate of progression of an individual patient. Importantly, the model also accounted for the perimetric floor effect by treating the distribution of sensitivity values as censored at 0 dB.[24,25] This prevents biasing the estimates of progression in patients with advanced VF loss toward slower rates. A similar approach was taken for the VFQ-25 composite score, modelling its linear change over time.

The main outcome measure was the estimated average rate of change (slope) and baseline (intercept) for the index eye VF, BI VF, and VFQ-25 score, modelled as a joint multivariable normal distribution at the patient level, explicitly quantifying the correlations among the 3 outcome measures. This also provided a more robust estimate of the parameters for each outcome measure. For example, the estimated slope of change in VFQ-25 score was informed by the change in index eye VF and BI VF and vice versa. Moreover, rates for patients with missing data can be inferred by the model using the estimated correlations. This maximizes the number of patients who can be included in the analysis and was necessary for 6 patients with missing VF data and 6 patients with

missing VFQ-25 data. In total, 10 patients were excluded because of insufficient VF and QoL data. The model was used to test for evidence of a difference between the rate of change of each outcome measure in the 2 arms of the trial. A Bayesian equivalent of the P value was calculated according to Makowski et al,[31] similarly to our previous publications.[25,32] Statistical significance was defined as a Bayesian P value of less than 0.05.

We performed a set of exploratory analyses. A secondary analysis was performed by replacing the composite score with the scores for the individual subscales. This version of the model estimated the correlations among all subscales and between the VF outcomes and the individual subscales.

Finally, we used a similar approach to model the correlations between individual locations of the BI VF and the VFQ-25 scores, characterizing the regional effects of BI VF damage and progression on QoL. Technical details of these models are reported in the Appendix. The same analyses were repeated using the calibrated Rasch logit scores for the VFQ-25 data (described and reported in the Appendix).

Results

Baseline descriptive statistics for the TAGS participants have been reported elsewhere.[17,18,26] Table 1 summarizes relevant baseline characteristics for the participants included in this analysis. The better eye was split evenly between right (n = 211) and left (n = 231) eyes.

The rate of progression of the index eye VF over 5 years was 0.37 dB/year (95% credible interval [CrI], 0.15−0.59 dB/year) slower in the trabeculectomy arm ($P = 0.002$). The rate of change for the BI VF and VFQ-25 composite score was slower in the trabeculectomy arm, but the differences were not significant. These results are summarized in Table 2.

The estimated VFQ-25 score baselines and rates of change were correlated positively with the estimated baselines and rates of change of both the BI VF and the index eye VF ($P < 0.001$; Fig 1). The correlations were stronger for the BI VF than for the index eye VF; this difference was significant for the estimated baselines ($P < 0.001$) and was borderline for the estimated rates of change ($P = 0.051$). A significant correlation was found between the BI VF and index eye VF in both estimated baselines (0.50 [95% CrI, 0.42−0.57]; $P < 0.001$) and rates of change (0.68 [95% CrI, 0.56−0.77]; $P < 0.001$). The partial correlation between index eye VF and VFQ-25 composite score, that is, the residual correlation after the correlation between the BI VF and index eye VF was taken into account, was much smaller and not significant (estimated baselines: 0.03 [95% CrI, −0.08 to 0.13; $P = 0.638$]; rates of change: 0.07 [95% CrI, −0.14 to 0.28; $P = 0.514$]).

Figure 2 shows the estimated baseline and rate of change correlations of the index eye VF and BI VF with VFQ-25 subscales. The BI VF estimated baselines and rates of progression showed stronger correlations with the VFQ-25 scores than the index eye VF. For both the estimated baselines and rates, the strongest correlation was for the driving subscale. The partial correlation for the index eye VF did not reach significance for any of the subscales. In the subscale model, the difference in the rate of VF progression between treatment arms for the index eye remained significant ($P = 0.002$), whereas no difference was found in estimated baseline and rates of change for either the BI VF or any of the subscales (Appendix). Similar results were obtained using the Rasch calibrated logit scores for the subscales; however, in this case, the difference in rate of progression for the BI VF was also borderline significant ($P = 0.048$; Appendix). The results were very similar in the analysis per protocol (Appendix), which also showed a significant difference in the BI VF rate of progression ($P = 0.034$).

Figure 3 reports the pointwise correlations for estimated baselines and rates of change between BI VF and the VFQ-25 composite score. The correlations generally were weaker than with the average BI VF, especially for the rates of change. The pointwise rates were correlated more strongly with the individual subscales. For the estimated baselines, the correlations were generally stronger in the inferior BI VF, especially in the central 10°. A weaker correlation was found at the blind-spot locations. This spatial pattern was less evident with the driving subscale. The rates of progression in the inferior and right BI VF seemed to be correlated more strongly with VFQ-25 rates of change. This pattern was more evident in the subscales. The correlations were more diffuse for the driving subscale. Similar patterns of correlations were obtained with the Rasch calibrated logit scores (Appendix).

Discussion

A significantly slower rate of VF deterioration for the index eye was found with trabeculectomy surgery compared with medications ($P = 0.002$). A similar trend was seen for the BI VF, but it did not reach statistical significance. No difference was found in the measure for vision-related QoL. However, the estimated baselines and rates of change of the VFQ-25 scores were correlated significantly with the estimated baselines and rates of progression of the BI VF and the monocular VF of the index eye, more strongly with the former.

The results are in agreement with the direction of the effect reported in our 2-year analysis[25] and with the significant difference in MD reported at 5 years.[18] Our current analysis provides a more accurate measurement of the rate of VF deterioration, exploiting rich information from pointwise VF data and minimizing the bias introduced by the perimetric floor effect.[24] This is crucial for accurate estimates in a population with advanced damage such as that in the TAGS.[25] We used VF sensitivity instead of age-corrected metrics. This allowed the modelling of the floor effect[25] and facilitated comparison with VFQ-25 scores, which are not age corrected. This does not affect the comparison between treatments, because aging would apply equally to participants in both arms, because of the randomized design. We focused on the index eye, rather than the better or worse eye, to estimate the maximal effect of treatment allocation. Because vision-related QoL is likely to correlate more strongly with binocular vision,[9,12,14,15] our methodology was extended to model the progression of BI VF and of

Table 1. Descriptive Statistics for the 2 Arms of the Trial for the Patients Included in This Analysis

Characteristic	Medications First		Trabeculectomy First	
	Index Eye (n = 221)	*Fellow Eye (n = 221)*	*Index Eye (n = 221)*	*Fellow Eye (n = 221)*
Age	70 (61–76)		68 (59–76)	
Sex				
Female	77 (35%)		71 (32%)	
Male	144 (65%)		150 (68%)	
Ethnicity				
Afro-Caribbean	27 (12%)		30 (14%)	
Asian	4 (1.8%)		10 (4.5%)	
White	186 (85%)		178 (81%)	
Other	3 (1.4%)		3 (1.4%)	
VFQ-25				
Composite score	91 (85–95)		91 (85–96)	
Follow-up (yrs)	5 (4–5)		5 (3–5)	
Questionnaires	7 (5–7)		7 (5–7)	
CCT (μm)	539 (517–565)	540 (520–563)	540 (517–560)	538 (517–564)
Lens status				
Phakic	205 (93%)	203 (92%)	206 (93%)	206 (93%)
Pseudophakic	16 (7.2%)	18 (8.1%)	15 (6.8%)	15 (6.8%)
IOP (mmHg)				
Diagnosis*	24.0 (20.0–32.0)	21.5 (18.0–26.5)	25.3 (21.0–32.0)	22.0 (18.8–26.0)
Baseline†	18.5 (15.5–21.5)	17.5 (15.0–20.5)	18.0 (15.3–22.0)	17.3 (14.0–21.0)
Visual acuity (logMAR)	0.10 (0.00–0.26)	0.04 (−0.04 to 0.14)	0.08 (0.00–0.24)	0.04 (−0.06 to 0.14)
Baseline MD (dB)	−13.5 (−19.7 to −10.9)	−3.7 (−7.7 to −1.3)	−13.7 (−18.2 to −10.7)	−3.9 (−7.9 to −1.3)
Baseline PSD (dB)	10.7 (9.0–12.5)	3.6 (2.1–7.6)	10.6 (9.1–12.7)	3.4 (2.2–7.5)
VF follow-up (yrs)	5 (2–5)	5 (2–5)	5 (2–5)	5 (2–5)
Included visits	5 (4–5)	5 (4–5)	5 (4–5)	5 (4–5)

CCT = central corneal thickness; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; MD = mean deviation; PSD = pattern standard deviation; VFQ-25 = Visual Function Questionnaire 25.
Data are presented as no. (%) or median (interquartile range).
*Before the initiation of treatment.
†After the initiation of medical treatment.

QoL metrics effectively. This provided a detailed description of the correlation between these outcome measures, offering insights to explain the results from the TAGS. The causal effect of treatment on QoL and VF progression was also investigated with a per-protocol analysis, because 26 participants (12%) in the trabeculectomy arm did not receive trabeculectomy in the index eye. The per-protocol analysis largely confirmed the results of the main intention-to-treat analysis (Appendix).

In agreement with previous reports of TAGS outcomes[17,18] and results from other randomized clinical trials,[16,19] standardized QoL instruments similar to the VFQ-25 were not able to identify a significant treatment effect, despite a strong impact of trabeculectomy on the rate of VF progression in the index eye. This is relevant especially in the context of the study design, which was powered to detect differences in QoL outcomes and measured QoL at more time points than the VF (see "Methods"). The failure

Table 2. Population Estimates (95% Credible Intervals) for the Estimated Baselines and Rates of Change in the 2 Arms of the Trial and Their Differences over 5 Years

Parameter	Medications First	Trabeculectomy First	Difference	*P* Value
Index eye VF				
Intercept (dB)	13.98 (12.96–15.00)	13.86 (12.83–14.88)	−0.12 (−1.57 to 1.35)	0.870
Slope (dB/yr)	−0.75 (−0.90 to −0.59)	−0.37 (−0.53 to −0.22)	0.37 (0.15–0.59)	0.002
Binocular integrated VF				
Intercept (dB)	25.35 (24.67–26.06)	25.10 (24.41–25.81)	−0.25 (−1.22 to 0.75)	0.619
Slope (dB/yr)	−0.40 (−0.51 to −0.29)	−0.25 (−0.36 to −0.14)	0.15 (−0.01 to 0.31)	0.062
VFQ-25 (composite score)				
Intercept (score)	87.22 (85.48–88.91)	86.47 (84.75–88.16)	−0.74 (−3.16 to 1.69)	0.544
Slope (score/yr)	−1.47 (−1.89 to −1.04)	−1.21 (−1.64 to −0.78)	0.26 (−0.35 to 0.85)	0.392

VF = visual field; VFQ-25 = 25-item Visual Function Questionnaire 25.

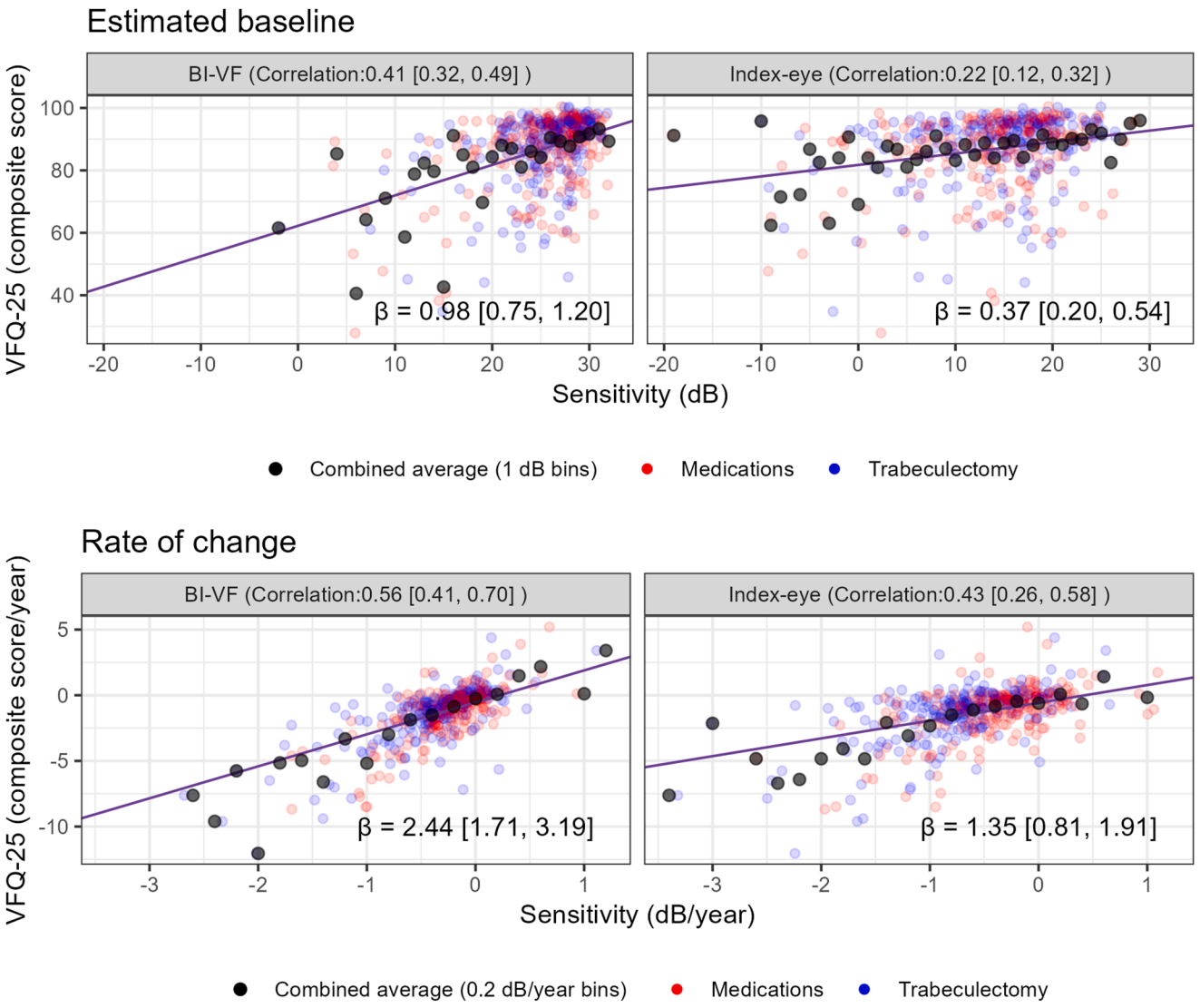

Figure 1. Scatterplots showing the patient-level estimates of the estimated baseline and rates of change for the joint longitudinal model for all patients in the cohort. The insets report the estimates and 95% credible intervals for the correlations. The black points and line represent the average trend for visual comparison with previous literature. Note that the estimated VF sensitivity can have negative values because of censoring. β = regression slope coefficient; BI = binocular integrated; VF = visual field; VFQ-25 = 25-item Visual Function Questionnaire.

to detect a difference is likely because vision-related QoL is determined mainly by binocular vision.[9,12,14,15,33] In the TAGS, the index eye most often corresponded to the worse VF eye (Table 1), whereas binocular vision would be dominated by the better-eye VF. We demonstrated this phenomenon by calculating the correlations for both the index eye and the BI VF and showing that the BI VF was correlated more strongly with QoL than the index eye VF (Table 2 and Fig 1). It should also be noted that the correlation between the index eye and the VFQ-25 is likely an indirect result of the correlation between index eye and the BI VF. This is demonstrated by the partial correlation for the index eye (i.e., the residual correlation between index eye VF and VFQ-25 score after accounting for the correlation between index eye VF and BI VF) being much lower and not statistically significant. The BI VF and better-eye analyses often provide similar results. However, in the TAGS, the worse eye was selected predominantly as the index eye. Therefore, modelling the better-eye VF would have removed the effect of the trial intervention systematically in most patients. However, we analyzed the subgroup of patients (n = 72) for whom the index eye was the better eye (Appendix). As expected, compared with the entire cohort, the index eye was correlated more strongly with the BI VF and the VFQ-25 score. However, the change in VFQ-25 was similar in this subgroup as well, showing no statistically significant difference.

A similar trend was observed with the individual VFQ-25 subscales (Fig 2; Appendix). No significant differences were found between trabeculectomy and medications in the rate of change for any of the subscales or the BI VF, although the difference remained strongly significant for

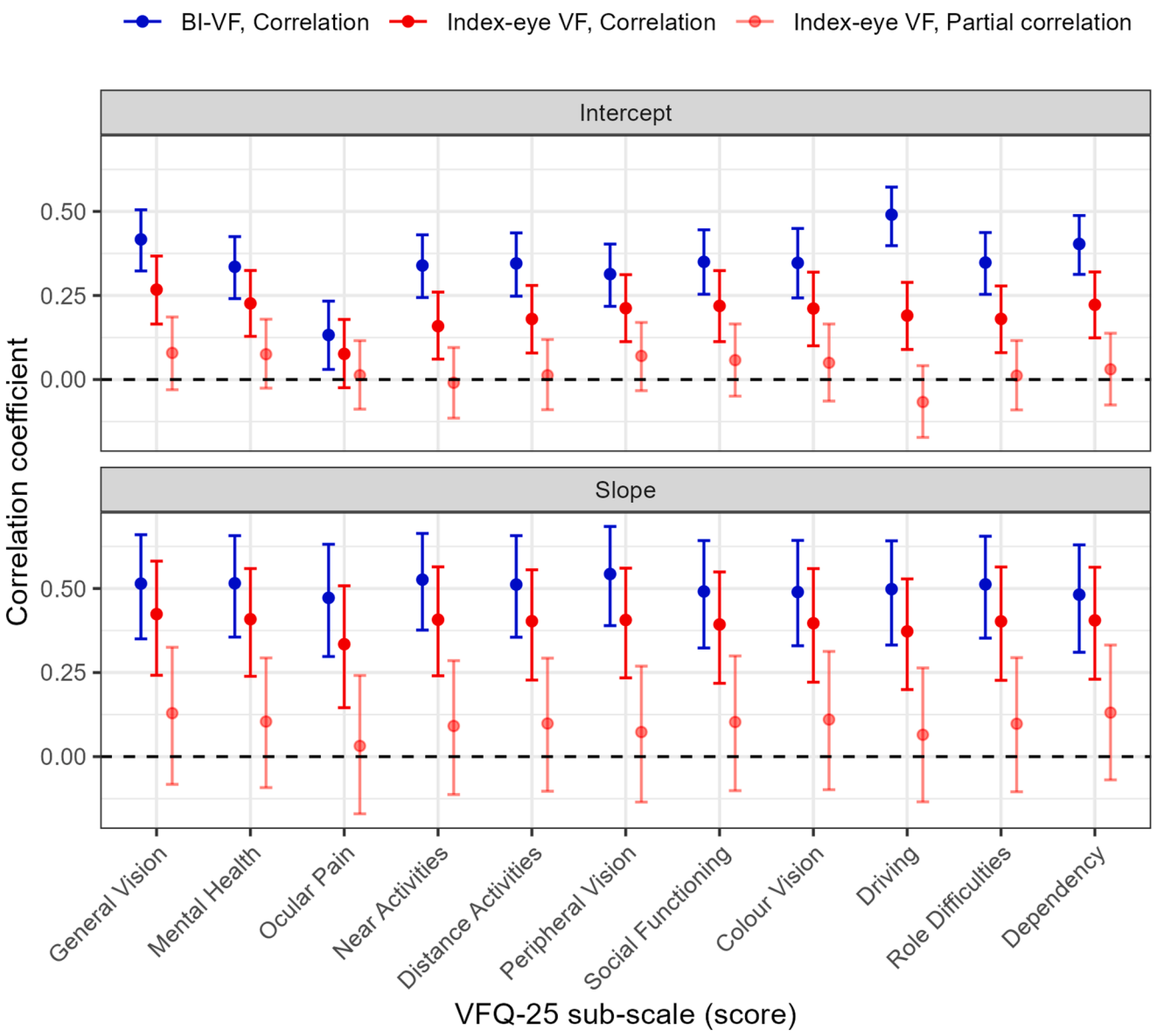

Figure 2. Graphs showing the estimated correlations (dots) and 95% credible intervals (bars) between estimated baselines and rates of progression of the index eye and binocular integrated (BI) visual field (VF) sensitivity with the estimated baselines and rates of change of the individual subscales. The shaded dots and bars represent the partial correlation for the index eye. VFQ-25 = 25-item Visual Function Questionnaire.

the index eye rate of VF progression ($P = 0.002$). The estimated baselines and rates of change for all subscales were correlated more strongly with the BI VF, with no significant partial correlations for the index eye VF. Importantly, despite some methodologic differences, the magnitude of the effect of VF loss on QoL (Fig 2) was very similar to previously reported values, for both the baseline damage[10] and the rates of change.[12] Also in agreement with previous literature,[11] the driving subscale was correlated most strongly with the BI VF. This scale was available for 343 patients in at least 1 questionnaire, with 22 patients reporting that they had stopped driving because of their eyesight at baseline and 51 patients stopping at some point during the follow-up. One limitation of our analysis is that we did not consider the informative censoring from patients who stopped driving. This, alongside a full characterization of other covariates that could influence QoL, will be the objective of future work. It is worth noting that no significant difference was found in the ocular pain and general health subscales between the surgery and medication arms. This makes it unlikely that non−vision-related effects of surgery determined the lack of a significant difference in vision-related QoL. These results are also in line with previous reports from the TAGS showing no significant difference, at baseline or throughout the trial, in general health scores, such as the one obtained with the EuroQol 5-Dimension 5-Level questionnaire.[18]

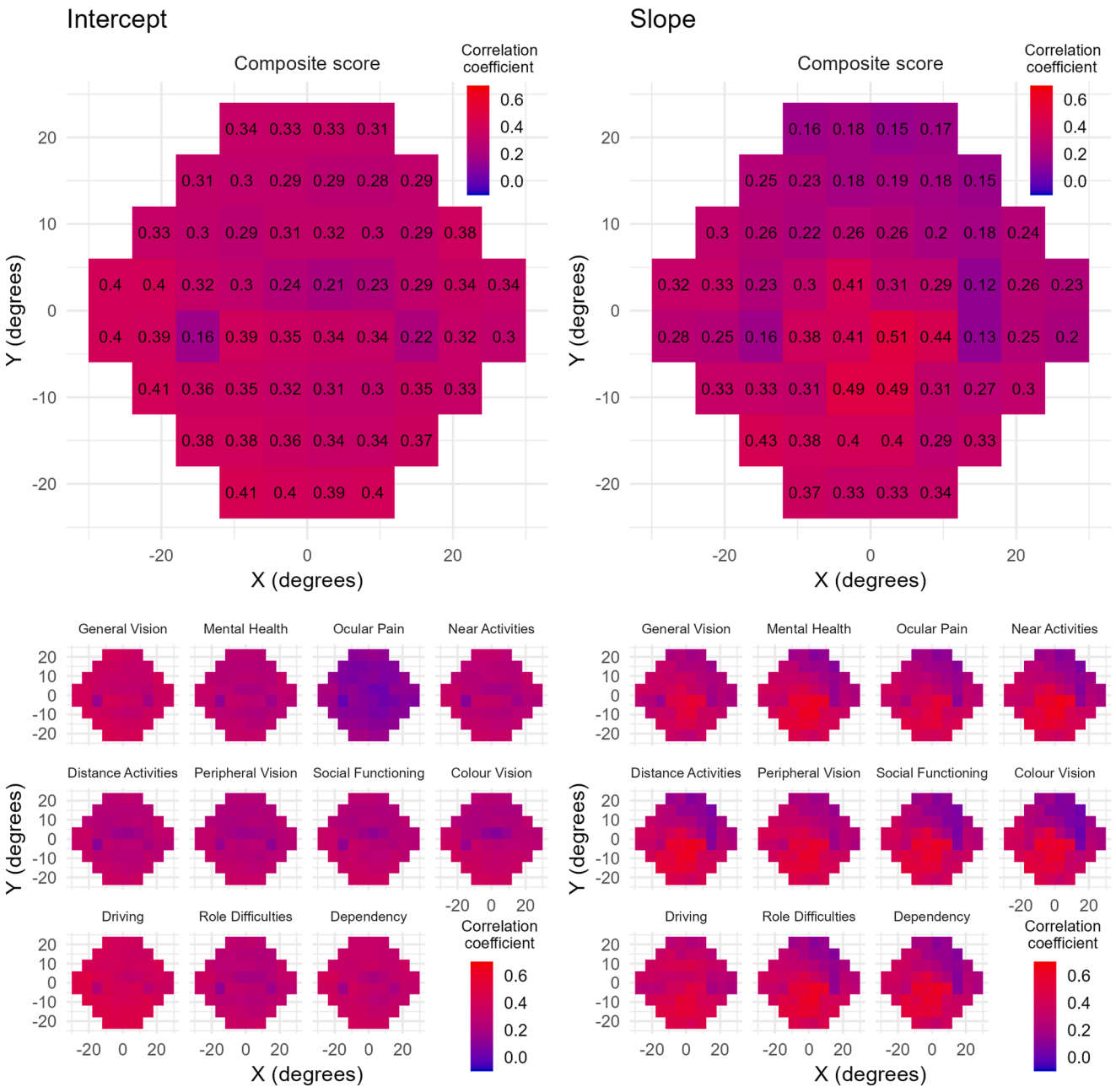

Figure 3. Diagrams showing the pointwise correlations between individual binocular integrated (BI) visual field (VF) locations and 25-item Visual Function Questionnaire scores (composites and subscales). The correlations for estimated baselines and rates of change are shown separately. The BI VF orientation is in patient view (the right side of the plot represents the patient's right hemifield).

We finally investigated the localized correlation between QoL and BI VF. The pointwise estimated baselines (Fig 3) showed generally stronger correlations in the inferior VF. This pattern was consistent across subscales. Regional association between VF loss and QoL are inconsistent in the literature, with reports of no regional patterns,[33] a stronger effect from the inferior VF,[15,34,35] or significant domain-specific correlations for different VF regions.[36] Excluding the blind-spot locations, the weakest correlations were found in the superior-paracentral VF, in agreement with previous findings.[36] Weaker correlations at the blind-spot locations are harder to explain, but could be related to either a differential processing of the information from this region of the VF, normally less sensitive even in the absence of pathologic features,[29,37] or could be a result of the uncertain estimation of the physiologic blind spots with standard automated perimetry.[38] A more diffuse pattern was noted for the driving and ocular pain subscales. The correlations for the pointwise rates were stronger in the inferior-left BI VF and within the central 10°. The stronger influence of central VF progression is in agreement with published literature[39] comparing central

and global VF loss estimated from 24-2 tests. Our analysis captures a similar effect but additionally accounts for the interaction between central and peripheral progression. The correlation of QoL with inferior VF progression has also been reported.[40] However, the significance of the left-right gradient has been explored poorly and remains unclear.[41] Future work also will focus on domain-specific BI VF reconstructions, especially for near or distance activities.[42] One limitation of our analysis is that it would not estimate the isolated contribution of each individual location. This can affect the measured correlations in different ways. On the one hand, locations that are affected earlier in the disease might be closer to the measurement floor at baseline, which would prevent a correct quantification of their rates of progression. However, this was not the case for the average baseline BI VF in the present cohort; in fact, locations in the superior hemifield showed, on average, faster rates of progression. These results are reported in the Appendix. However, the inferior BI VF might be correlated more strongly with QoL because these locations are affected later in the course of the disease, when the BI VF is more advanced globally, thus amplifying their impact. To address this aspect, we performed a supplementary analysis to quantify the partial correlation between the VFQ-25 composite score and the locations of the inferior or superior BI VF hemifield, conditional to the opposite hemifield. This is effectively measuring the pointwise correlations with QoL for varying intercepts and slopes in 1 hemifield, while holding the intercepts and slopes constant in the opposite hemifield, accounting for global long-range correlations. The pointwise partial correlations also confirmed our main findings (Appendix). Note that this analysis used the correlations between individual locations and with the VFQ-25 scores estimated by the same model used for the main analysis. Finally, the raw pointwise average BI VF sensitivity at the different time points, stratified by initial binocular average sensitivity, did not show a marked superior–inferior asymmetry that would justify the spatial patterns of correlation with QoL (Appendix).

Previous work has suggested that the relationship between VF loss and QoL might be nonlinear.[13] The linearity assumption was necessary because of the complex correlation structures in our model. However, it should be mentioned that the nonlinear behavior could be, at least partially, a consequence of the ceiling effect in the raw VFQ-25 scores, evident from the figures published in Jones et al.[13] We have repeated all our analyses using a logit score from a Rasch model (Appendix), which would remove this effect, with no meaningful differences in our results. This suggests that the assumption of linearity is likely adequate in our cohort.

These results are important because the goal of glaucoma treatment is often stated to be the maintenance of vision-related QoL.[43] The results confirm previous findings that VF measurements are more precise, more responsive, or both as clinical trial outcomes to identify treatment effects on glaucoma progression than measurements of vision-related QoL,[16,19] while also showing a significant and clinically meaningful correlation between VF progression and perceived changes in participants' vision-related QoL. This supports VF measurement as the more suitable primary outcome for clinical trials and underpins the importance of including QoL among secondary outcomes, especially because QoL instruments are able to capture adverse outcomes and non-VF effects of treatment.[44] Quality of life changes are also unlikely to be driven solely by VF change, because participants in the TAGS were aware of their treatment allocation and may have been aware of their progression status. These factors, in addition to VF change, may influence changes in QoL and also may explain, in part, previous similar findings.[12,16] The difference in QoL also might have been confounded by postoperative recovery and other intercurring factors, such as cataract development and medication burden. A description of these events has been presented extensively elsewhere.[18] It is important to note that ocular surface disease and cataract surgery had very similar incidence between the 2 arms and therefore are unlikely to have influenced the systematic differences in VF and QoL metrics in the TAGS.[18]

However, these results do not undermine the importance of the QoL measurements because they represent the participants' vision-related experience, as influenced by the effect of having glaucoma on both vision and anxiety, and the potentially positive[45] and adverse effects of glaucoma treatments that are not related to disease progression. In this respect, it is important to note that trabeculectomy surgery did not have a negative effect on QoL in the TAGS. Moreover, although VF results are more responsive than VFQ-25 scores for detecting treatment effects within a 5-year trial horizon, especially for monocular interventions, extensive longitudinal evidence shows that VF loss, particularly binocular and inferior-field decline, predicts deterioration in vision-related QoL, notably in driving ability.[14] These findings are complementary, rather than contradictory. Longer observation periods could show the long-term effect of treatment on QoL. In the TAGS, the minimally clinically important difference was set at 6 points for the composite score,[17,18] in agreement with previous literature in similar populations.[46,47] Using our estimates (Table 2), it would take 23 years to show such a difference on average. Such a long observation period is impractical for clinical trials. Moreover, patients who are identified as showing deterioration based on clinical metrics (such as VF) would warrant earlier additional treatment, preventing the measurement of the intended QoL outcome. In contrast, a difference in reaching commonly used clinical threshold of 2-dB VF mean sensitivity or MD change[46] would be achieved in 5.4 years for the index eye.

In conclusion, trabeculectomy was more effective than drops in preserving VF and should be considered as a first treatment in patients with advanced glaucoma. No difference was found in measured QoL between the 2 arms, despite a strong correlation between VFQ-25 scores and BI VF loss. Therefore, current QoL instruments are likely not precise or responsive enough to the effect of glaucoma treatment to be used as the primary outcome measure in randomized clinical trials.

Footnotes and Disclosures

Originally received: December 18, 2025.
Final revision: March 23, 2026.
Accepted: April 7, 2026.
Available online: April 24, 2026. Manuscript no. OPHTHA-D-25-03066.

[1] NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom.

[2] Optometry and Visual Sciences, City St George's, University of London, London, United Kingdom.

[3] School of Pharmacy, Optometry & Medical Sciences, University of Bradford, Bradford, United Kingdom.

[4] Nottingham University Hospital, Nottingham, United Kingdom.

Disclosure(s):

All authors have completed and submitted the ICMJE disclosures form.

The author(s) have made the following disclosure(s):

G.M.: Consultant — CenterVue, Omikron, Alcon, Enavate Science, Perfuse Therapeutics, Théa, Astellas, Vialase; Financial support — Santen, Omikron, Théa, Glaucoma UK; Nonfinancial support — Santen; Leadership or fiduciary role — Relayer; Lecturer — Omikron, Théa

G.O.: Consultant — Alcon, Precision Vision, Vialase; Leadership or fiduciary role — Relayer; Financial support — Glaucoma UK

D.F.G.-H.: Consultant — AbbVie, CenterVue, Janssen, Santen, Omikron; Financial support — Alcon Research Institute, Janssen, Santen, Viatris, Glaucoma Research Foundation; Lecturer — Novartis, Topcon; Nonfinancial support — CentreVue Revenio, Topcon

D.P.C.: Financial support — AbbVie/Allergan, Apellis, Santen; Consultant — AbbVie/Allergan, Apellis, Thèa, Santen, Glaukos, Janssen; Nonfinancial support — Santen

A.J.K.: Lecturer — Thèa; Data Safety Monitoring Board or Advisory Board — Santen, AbbVie, SightSciences; Fiduciary role — Glaucoma UK

Supported by Glaucoma UK (2023 Royal College of Ophthalmologists/Glaucoma UK research grant [G.M.], D.G.-H.'s chair at UCL); and the National Institutes of Health, Bethesda, Maryland (grant no.: EY034554 [D.C., B.H., R.C.]).

The Article Publishing Charge (APC) for this article was paid via an agreement between Elsevier and UCL.

The full list of group members in the TAGS Study Group is available at www.aaojournal.org.

HUMAN SUBJECTS: Human subjects were included in this study. The study was approved by the East Midlands Derby Research Ethics Committee (reference no., 13/EM/0395; registration no., ISRCTN56878850) and adhered to the tenets of the Declaration of Helsinki. All patients provided written informed consent.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Montesano, Cheloni, Garway-Heath, Crabb, King

Analysis and interpretation: Montesano, Cheloni, Garway-Heath, Crabb, King

Data collection: Montesano, Ometto, Cheloni, Higgins, King

Obtained funding: King

Overall responsibility: Montesano, Ometto, Cheloni, Garway-Heath, Higgins, Crabb, King

Abbreviations and Acronyms:
BI = binocular integrated; **CrI** = credible interval; **FPR** = false-positive rate; **MD** = mean deviation; **QoL** = quality of life; **SITA** = Swedish Interactive Thresholding Algorithm; **TAGS** = Treatment for Advanced Glaucoma Study; **VF** = visual field; **VFQ-25** = 25-item Visual Function Questionnaire.

Keywords:
Glaucoma, Quality of life, Trabeculectomy, VFQ-25, Visual field.

Correspondence:
Giovanni Montesano, MD, PhD, NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London EC1V 2PD, United Kingdom. E-mail: g.montesano@ucl.ac.uk.

References

1. Wilson R, Walker AM, Dueker DK, Crick RP. Risk factors for rate of progression of glaucomatous visual field loss: a computer-based analysis. *Arch Ophthalmol*. 1982;100:737–741.
2. Lee JM, Caprioli J, Nouri-Mahdavi K, et al. Baseline prognostic factors predict rapid visual field deterioration in glaucoma. *Invest Ophthalmol Vis Sci*. 2014;55:2228–2236.
3. Mokhles P, Schouten JSAG, Beckers HJM, et al. A systematic review of end-of-life visual impairment in open-angle glaucoma: an epidemiological autopsy. *J Glaucoma*. 2016;25:623–628.
4. Saunders LJ, Russell RA, Kirwan JF, et al. Examining visual field loss in patients in glaucoma clinics during their predicted remaining lifetime. *Invest Ophthalmol Vis Sci*. 2014;55:102–109.
5. Ernest PJG, Busch MJWM, Webers CAB, et al. Prevalence of end-of-life visual impairment in patients followed for glaucoma. *Acta Ophthalmol*. 2013;91:738–743.
6. Kastner A, King AJ. Advanced glaucoma at diagnosis: current perspectives. *Eye (London)*. 2020;34:116–128.
7. Kulkarni BB, Leighton P, King AJ. Exploring patients' expectations and preferences of glaucoma surgery outcomes to facilitate healthcare delivery and inform future glaucoma research. *Br J Ophthalmol*. 2019;103:1850–1855.
8. Bhargava JS, Bhan-Bhargava A, Foss AJE, King AJ. Views of glaucoma patients on provision of follow-up care; an assessment of patient preferences by conjoint analysis. *Br J Ophthalmol*. 2008;92:1601–1605.
9. Peters D, Heijl A, Brenner L, Bengtsson B. Visual impairment and vision-related quality of life in the early manifest glaucoma trial after 20 years of follow-up. *Acta Ophthalmol*. 2015;93:745–752.
10. McKean-Cowdin R, Varma R, Wu J, et al. Severity of visual field loss and health-related quality of life. *Am J Ophthalmol*. 2007;143:1013–1023.
11. Grisafe DJ, McKean-Cowdin R, Burkemper BS, et al. Visual field loss impacts vision-specific quality of life by race and ethnicity: the Multiethnic Ophthalmology Cohorts of California study. *Ophthalmology*. 2022;129:668–678.
12. Medeiros FA, Gracitelli CPB, Boer ER, et al. Longitudinal changes in quality of life and rates of progressive visual field loss in glaucoma patients. *Ophthalmology*. 2015;122:293–301.

13. Jones L, Bryan SR, Crabb DP. Gradually then suddenly? Decline in vision-related quality of life as glaucoma worsens. *J Ophthalmol*. 2017;2017:1621640.
14. Lisboa R, Chun YS, Zangwill LM, et al. Association between rates of binocular visual field loss and vision-related quality of life in patients with glaucoma. *JAMA Ophthalmol*. 2013;131:486–494.
15. van Gestel A, Webers CAB, Beckers HJM, et al. The relationship between visual field loss in glaucoma and health-related quality-of-life. *Eye (London)*. 2010;24:1759–1769.
16. Jones L, Garway-Heath DF, Azuara-Blanco A, Crabb DP. Are patient self-reported outcome measures sensitive enough to be used as end points in clinical trials? Evidence from the united kingdom glaucoma treatment study. *Ophthalmology*. 2019;126:682–689.
17. King AJ, Hudson J, Fernie G, et al. Primary trabeculectomy for advanced glaucoma: pragmatic multicentre randomised controlled trial (TAGS). *BMJ*. 2021;373:n1014.
18. King AJ, Hudson J, Azuara-Blanco A, et al. Evaluating primary treatment for people with advanced glaucoma: five-year results of the treatment of advanced glaucoma study. *Ophthalmology*. 2024;131:759–770.
19. Hyman LG, Komaroff E, Heijl A, et al. Treatment and vision-related quality of life in the early manifest glaucoma trial. *Ophthalmology*. 2005;112:1505–1513.
20. Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol*. 2001;119:1050–1058.
21. Richman J, Lorenzana LL, Lankaranian D, et al. Relationships in glaucoma patients between standard vision tests, quality of life, and ability to perform daily activities. *Ophthalmic Epidemiol*. 2010;17:144–151.
22. Guedes RAP, Guedes VMP, Freitas SM, Chaoubah A. Quality of life of medically versus surgically treated glaucoma patients. *J Glaucoma*. 2013;22:369–373.
23. Wu P, Xi S, Xia H, et al. Survey on vision-related quality of life and self-management among patients with glaucoma. *J Glaucoma*. 2014;23:75–80.
24. Montesano G, Garway-Heath DF, Ometto G, Crabb DP. Hierarchical censored bayesian analysis of visual field progression. *Transl Vis Sci Technol*. 2021;10:4.
25. Montesano G, Ometto G, King A, et al. Two-year visual field outcomes of the treatment of advanced glaucoma study (TAGS). *Am J Ophthalmol*. 2023;246:42–50.
26. King AJ, Hudson J, Fernie G, et al. Baseline characteristics of participants in the treatment of advanced glaucoma study: a multicenter randomized controlled trial. *Am J Ophthalmol*. 2020;213:186–194.
27. Damji KF, Behki R, Wang L. Canadian perspectives in glaucoma management: setting target intraocular pressure range. *Can J Ophthalmol*. 2003;38:189–197.
28. Yohannan J, Wang J, Brown J, et al. Evidence-based criteria for assessment of visual field reliability. *Ophthalmology*. 2017;124:1612–1620.
29. Nelson-Quigg JM, Cello K, Johnson CA. Predicting binocular visual field sensitivity from monocular visual field results. *Invest Ophthalmol Vis Sci*. 2000;41:2212–2221.
30. Heijl A, Patella VM, Flanagan JG, et al. False positive responses in standard automated perimetry. *Am J Ophthalmol*. 2022;233:180–188.
31. Makowski D, Ben-Shachar MS, Chen SHA, Lüdecke D. Indices of effect existence and significance in the bayesian framework. *Front Psychol*. 2019;10:2767.
32. Montesano G, Ometto G, Ahmed IIK, et al. Five-year visual field outcomes of the HORIZON trial. *Am J Ophthalmol*. 2023;251:143–155.
33. Jampel HD, Friedman DS, Quigley H, Miller R. Correlation of the binocular visual field with patient assessment of vision. *Invest Ophthalmol Vis Sci*. 2002;43:1059–1067.
34. Cheng H-C, Guo C-Y, Chen M-J, et al. Patient-reported vision-related quality of life differences between superior and inferior hemifield visual field defects in primary open-angle glaucoma. *JAMA Ophthalmol*. 2015;133:269–275.
35. Takizawa Y, Ro T, Murono M, et al. The impact of inferior visual field on frail status in glaucoma patients. *Int Ophthalmol*. 2025;45:168.
36. Chun YS, Sung KR, Park CK, et al. Vision-related quality of life according to location of visual field loss in patients with glaucoma. *Acta Ophthalmol*. 2019;97:e772–e779.
37. Wood JM, Collins MJ, Carkeet A. Regional variations in binocular summation across the visual field. *Ophthalmic Physiol Opt*. 1992;12:46–51.
38. Wang M, Shen LQ, Boland MV, et al. Impact of natural blind spot location on perimetry. *Sci Rep*. 2017;7:6143.
39. Gunasegaran G, Moghimi S, Walker E, et al. Differential impact of central and global visual field progression on quality of life in glaucoma. *Am J Ophthalmol*. 2025;276:327–335.
40. Abe RY, Diniz-Filho A, Costa VP, et al. The impact of location of progressive visual field loss on longitudinal changes in quality of life of patients with glaucoma. *Ophthalmology*. 2016;123:552–557.
41. Murata H, Hirasawa H, Aoyama Y, et al. Identifying areas of the visual field important for quality of life in patients with glaucoma. *PloS One*. 2013;8:e58695.
42. Liu P, McKendrick A, Ma-Wyatt A, Turpin A. A depth-dependent integrated VF simulation for analysis and visualization of glaucomatous VF defects. *Transl Vis Sci Technol*. 2020;9:8.
43. Society EG. European Glaucoma Society terminology and guidelines for glaucoma, 5th edition. *Br J Ophthalmol*. 2021;105:1–169.
44. Rabiolo A, Barton K, McNaught AI. Patient-reported outcome measures should not be the primary outcome in glaucoma clinical trials of disease modification. *Br J Ophthalmol*. 2023;107:3–5.
45. Azuara-Blanco A, Burr J, Ramsay C, et al. Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial. *Lancet*. 2016;388:1389–1397.
46. Kotecha A, Feuer WJ, Barton K, Gedde SJ. Quality of life in the tube versus trabeculectomy study. *Am J Ophthalmol*. 2017;176:228–235.
47. Burr JM, Cooper D, Ramsay CR, et al. Interpretation of change scores for the national eye institute visual function questionnaire-25: the minimally important difference. *Br J Ophthalmol*. 2022;106:1514–1519.